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Water-drinking test and its importance in glaucoma management

Teste de Sobrecarga Hídrica e sua importância no manejo do glaucoma

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RESUMO

O teste de sobrecarga hídrica (TSH) foi descrito pela primeira vez como uma ferramenta de diagnóstico para o glaucoma, sendo posteriormente abandonado devido sua baixa precisão diagnóstica. Este teste tem ganhado significante interesse nos últimos anos, uma vez que diferentes estudos têm mostrado a sua utilização como um substituto para a detecção de pacientes com picos de PIO não detectados durante o horário regular de expediente. De acordo com a literatura revisada por pares, o pico de PIO detectado pelo TSH correlaciona-se positivamente com a gravidade de defeitos de campo visual no glaucoma e podem ser preditivos para progressão de campo visual. Demonstrou-se que os picos de PIO durante o TSH estão correlacionados e de acordo com picos de PIO que normalmente ocorrem durante o dia. O TSH também foi usado para avaliar a qualidade de diferentes opções clínicas e cirúrgicas no glaucoma. O principal objetivo desta revisão é apresentar e discutir tais evidências e a aplicabilidade do TSH como uma ferramenta de avaliação para a doença glaucomatosa.

Palavras-Chave:
Pressão intra-ocular
Dinâmica do humor aquoso
Glaucoma
Teste de estresse

ABSTRACT

Water-drinking test (WDT) was first described as a diagnostic tool for glaucoma; however, it was later abandoned because of its poor diagnostic accuracy. This test has gained significant attention in recent years because different studies have shown its use as a surrogate for detecting patients who have intraocular pressure (IOP) spikes not measured during regular office hours. According to the peer-reviewed literature, IOP peaks detected by the WDT positively correlate with the severity of visual field defects in glaucoma and may predict visual field progression. Furthermore, it was demonstrated that IOP peaks detected by the WDT were correlated and in agreement with the IOP peaks that normally occurred during the day. The WDT is also used to evaluate the quality of different clinical and surgical treatment options in glaucoma. The main objective of this review was to present and discuss the evidence and applicability of the WDT as an assessment tool for glaucoma.

Keywords:
Intraocular Pressure
Aqueous Humor Dynamics
Glaucoma
Stress Testing

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INTRODUCTION

Elevated intraocular pressure (IOP) is considered the main risk factor for the development and progression of glaucoma[1, 2, 3]. To date, treatment options are mainly based on the reduction of IOP to a level at which no additional damage is expected to occur. This pressure level, frequently referred to as the target IOP, is established on individual basis and is typically assessed by single office measurements during working hours.

Despite maintaining apparently well-controlled IOP levels, some patients continue to develop glaucoma progression. Although some authors state that this may be a result of IOP fluctuation[4, 5, 6], **recent studies have demonstrated that peak IOP is a better predictor of glaucoma progression**[7, 8, 9].

Twenty-four hour pressure monitoring could be considered the best way to assess the IOP profile and detect peaks during pressure. However, this procedure is a time- and resource-consuming procedure and is not always feasible in routine practice. As an alternative, many clinicians have frequently used the modified diurnal tension curve (mDTC), which consists of four to five IOP measurements that are taken during office hours (from 8 am to 6 pm). However, as demonstrated by Drance[10], one-third of patients with IOP measurements taken during office hours may present pressure peaks which would only be detected during a 24-h diurnal tension curve (DTC). According to the results by Barkana et al.[11], a complete IOP evaluation over a 24-h period may reveal higher peaks than those revealed by measurements taken during office hours in 62% of patients, resulting in a treatment change for 36% of the patients in their study sample.

In this context, the WDT has been proposed as a practical alternative for the evaluation of IOP profiles of patients with glaucoma.

The WDT was first described a few decades ago for the diagnosis of open-angle glaucoma; however, it was later abandoned because of its high level of false-positive and false-negative results[12,13] and lack of diagnostic value[14]. Recently, this test was revived for new purposes: it has been used as a surrogate marker for outflow facility reserve and may be an indicator for the likelihood of progression[15,16].

These new concepts led to a growing interest in the test. The WDT has recently been the subject of three editorials in peer-reviewed journals[17,18,19]. In an editorial about publication and citation in ophthalmology, the authors stated that the WDT had experienced a major and recent revival based on the fact that the 32 articles that included this test have been cited 10.26 times (range 10–49), which is a mean citation count above the normal and expected mean[17].

In this low-cost and clinically-applicable examination, eligible patients (i.e., those who are not on fluid restriction because of systemic conditions) are instructed not to drink during the 2-h period before the WDT. The patient's baseline IOP is then measured and the patient is required to drink 1000 of water in 5 min. Next, the IOP is measured three additional times at 15-min intervals[20]. The baseline IOP is the IOP value measured immediately before water ingestion. The maximum value of the three measurements is selected as the peak IOP during the WDT. This increase in IOP is reversible and usually lasts for only a few minutes; furthermore, the WDT is not typically believed to be harmful to patients. Research has shown that the peaks that were obtained by this test strongly correlated and were in agreement with the IOP peaks that normally occurred during the day[21,22,23]. Moreover, it may be observed that eyes with higher IOP peaks after water ingestion may take longer to return to baseline IOP levels[11], which may reflect the status of the drainage system of the eye.

One direct comparison between the ingestion of 1000 mL (33.8 ounces) or 500 mL (16.9 ounces) of water demonstrated that the latter failed to estimate the peak diurnal pressure[24]. **It has been suggested that the WDT may be performed with 800 mL (27.0 ounces) of water** (R. Susanna Jr., personal communication), leading to similar results. Stamper et al. [Stamper R et al: The relationship between progression of glaucoma and supine and WDT. World Glaucoma Congress, Boston MA, 2009 (P 282)] showed that the peak of the WDT elicited when using 800 mL of water was significantly associated with the progression of open-angle glaucoma. It seems that 800 mL may be used instead of 1000 mL; however, further studies are necessary to evaluate results with this volume of water. Other researchers have evaluated the use of 10 mL of water/kg of weight as the WDT study volume[25].

The mechanism of the IOP increase after a water overload remains unclear. A recent study suggested that it was caused, at least in part, by the expansion of the choroidal tissue. The increase in choroidal volume would then be transmitted to the intraocular compartments and to the anterior segment of the eye[26]. Because an eye may display either a higher or lower IOP elevation depending on the status of its outflow facility[27], WDT may function as a stress test for the evaluation of the aqueous humor outflow facility. This finding was not supported by a study by Quigley[28]. The elevation of IOP has also been reported to be a consequence of an increase in the episcleral venous pressure[29].

Despite the lack of knowledge about the mechanism of the IOP increase during the test, several studies have shown the clinical application and importance of the WDT in the management of primary open angle glaucoma. The WDT was used to compare the effects of different clinical and surgical treatment modalities in glaucoma. Medically controlled patients with glaucoma have a greater IOP increase

with the WDT than patients who have undergone a filtration surgery such as trabeculectomy[30] or deep sclerectomy[31], despite similar mean IOPs at baseline. This behavior may be caused by the fact that filtering procedures facilitate aqueous humor outflow more effectively than medical therapy. In a study where a 24-h DTC was performed in patients with maximum medical treatment and in patients who had a trabeculectomy, 37% of patients in the medically-treated group showed IOP measurements of >18 mmHg, whereas none of the surgically-treated patients showed such an increase[32]. These results were parallel to the findings of Danesh-Meyer et al.[30] who demonstrated that 30% of patients under clinical treatment had an IOP that was >18 mmHg after the WDT compared to no such increase in IOP in the trabeculectomy group.

The same rationale may be used to understand the application of the WDT to assess to the efficacy of different hypotensive medications for glaucoma. In a comparison between latanoprost and the fixed combination of dorzolamide and timolol, patients who received latanoprost showed significantly smaller elevations in their IOP levels following the WDT. The authors surmised that the dampening effect on the IOP elevation in the latanoprost group was a result of this agent's mechanism of action, i.e., an increase in uveoscleral outflow[33]. Similarly, Vetrugno et al.[34] demonstrated that prostaglandin analogues and alpha agonists, which improve outflow, are associated with better IOP stabilization during a WDT in comparison to drugs that decreased aqueous humor production, such as -blockers and carbonic anhydrase inhibitors. **Drugs that show a similar mean IOP reduction but better ability to avoid IOP peaks may have an additional benefit on glaucoma treatment.**

The WDT may be used to assess the efficacy of an ocular hypotensive therapy or treatment. Malerbi et al.[35] analyzed the results of the mDTC and WDT in a series of 65 eyes of 65 patients who had achieved predetermined target IOPs based on their levels of glaucomatous damage (IOP ≤15 mmHg) at single office readings. mDTC revealed IOP measurements >18 mmHg in 13.8% of eyes, with 20 mmHg as the highest detected IOP. The WDT demonstrated that 33.8% of eyes presented with peaks >18 mmHg. Moreover, this test even depicted IOP levels of >20 mmHg in 21.5% of the tested eyes.

In 101 patients with open-angle glaucoma and asymmetric visual field defects, the eyes that had worse mean deviation (MD) values had higher IOP peaks after water ingestion in comparison with their contralateral eyes that had better visual fields despite similar mean baseline IOPs (Fig. 2). This study demonstrated a lower capacity of eyes with more significant damage due to glaucoma for controlling pressure[16]. An increase of 1 mmHg in the IOP is associated with a 10% increase in the relative risk for glaucoma conversion[1] and visual field progression[3,36]. Another study performed by the same group of investigators analyzed the IOP profile after WDT and concluded that the mean IOP peak and the percentage of IOP variation during the test were significantly higher in patients with visual field progression compared with patients who did not show visual field progression[15], despite the same baseline IOPs (Figs. 3 and 4).

Previous studies have also found a correlation between the WDT response and progressive damage. In a prospective study of 5,000 patients with open-angle glaucoma, Armaly et al.[37] identified 5 of 26 potential risk factors that were significantly related to the development of visual field defects: outflow facility, age, IOP, cup-to-disc ratio, and the change in IOP after water ingestion. In a sample of normotensive glaucomatous patients evaluated by Yoshikawa et al.[38], the WDT was the main predictive test for glaucoma progression.

To be considered clinically applicable, a test must present reproducible results. When performed at the same time of the day on two consecutive days, Hatanaka et al.[40] demonstrated that the IOP peaks during the WDT presented excellent reproducibility (ICC = 0.79, $p < 0.001$)[40]. The IOP results were also similar when performed at 4 months apart at same time of the day[39].

CONCLUSION

There has been an increased value attributed to the occurrence of IOP peaks as risk factors for glaucoma progression[8,41], and more interest has been observed in establishing a target IOP peak or target IOP peak range pressure instead of a single target IOP. Therefore, future studies regarding methods for better evaluation of the IOP profile over a 24-h period will be warranted. Special devices for continuous IOP monitoring are currently under analysis. However, their practical use on a daily basis and in high-volume outpatient settings over a short-term period is uncertain. The measurements given by the trigger, fish lens device, have not corresponded to the IOP measured in mmHg and also can be influenced by central cornea thickness and hysteresis. Some side effects such as corneal edema, hyperemia, and discomfort have also been associated with its use. Meanwhile, the WDT with reproducible and clinically significant

results that have been validated several times by peer-reviewed studies can be an important tool for IOP profile assessment in glaucoma management.

It is important to stress that the WDT cannot be used for the diagnosis of glaucoma, but can be used to assess the IOP profile of a given patient. Thus, there are no positive or negative values for this test. The WDT may also be used as a stress test to evaluate the ability of the eye to deal with transient IOP elevation and to assess the quality of hypotensive treatment. High IOP peaks during the WDT may also be considered a risk factor for glaucomatous damage and progression.

The best practical way to assess if the IOP of a given patient is in the target peak range is to perform the WDT. It is also the best way to compare the efficacy of hypotensive medications to dump IOP spikes.

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